Amendments to the Specification:

Please amend the paragraph on page 6, beginning on line 18 to read as follows:

Figure 13. Alanine scanning mutagenesis of the C-terminally derived PTP HSCF peptide. Peptides derived from the C-terminus of PTP HSCF with alanines at each of the indicated positions were analyzed for their ability to inhibit the interaction between in vitro transcribed and translated PST PIP and the GST PTP HSCF fusion protein. Inhibition of the interaction results in a loss of binding to the GST fusion and a lack of signal on the gel, while peptides with decreased inhibitory activity are poorly competitive and allow for binding. Also illustrated is the sequence of this C-terminal region in the peptide used for this analysis, PTP HSCF (SEQ ID NO: 74) (Cheng *et al.* (1996), *supra* as well as PTP PEST (SEQ ID NO: 75) (Garton and Tonks, *EMBO J.* 13(16):3763-3771 (1994)) and PTP PEP (SEQ ID NO: 76) (Matthews *et al.* (1992), *supra*).

Please amend the paragraph on page 18, beginning on line 4 to read as follows:

Other cloning and expression vectors suitable for the expression of the PSTPIP polypeptides of the present invention in a variety of host cells are, for example, described in EP 457,758 published 27 November 1991. A large variety of expression vectors are now commercially available. An exemplary commercial yeast expression vector is pPIC.9 (~~Invitrogen~~ Invitrogen™), while an commercially available expression vector suitable for transformation of E. coli cells is PET15b (~~Novagen~~ Novagen™).

Please amend the paragraph on page 18, beginning on line 12 to read as follows:

Mammalian cells can be cultured in a variety of media. Commercially available media such as Ham's FIO (~~Sigma~~ Sigma™), Minimal Essential Medium (MEM, ~~Sigma~~ Sigma™), RPMI-1640 (Sigma), and Dulbecco's Modified Eagle's Medium (DMEM, ~~Sigma~~ Sigma™) are suitable for culturing the host cells. In addition, any of the media

described in Ham and Wallace, *Meth. Enzymol.* 58:44 (1979); Barnes and Sato, *Anal. Biochem.* 102:255 (1980), US 4,767,704; 4,657,866; 4,927,762; or 4,560,655; WO 90/03430; WO 87/00195 or US Pat. Re. 30,985 may be used as culture media for the host cells. Any of these media may be supplemented as necessary with hormones and/or other growth factors (such as insulin, transferrin, or epidermal growth factor), salts (such as sodium chloride, calcium, magnesium, and phosphate), buffers (such as HEPES), nucleosides (such as adenosine and thymidine), antibiotics (such as Gentamycin™ drug) trace elements (defined as inorganic compounds usually present at final concentrations in the micromolar range), and glucose or an equivalent energy source. Any other necessary supplements may also be included at appropriate concentrations that would be known to those skilled in the art. The culture conditions, such as temperature, pH and the like, suitably are those previously used with the host cell selected for cloning or expression, as the case may be, and will be apparent to the ordinary artisan.

Please amend the paragraph on page 30, beginning on line 25 to read as follows:

Preferred myeloma cells are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. Among these, preferred myeloma cell lines are murine myeloma lines, such as those derived from MOPC-21 and MPC- I I mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, California USA, and SP-2 cells available from the American Type Culture ~~Collection~~ Collection™, Rockville, Maryland USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, *J. Immunol.* 133:3001 (1994); Brodeur et al., *Monoclonal Antibody Production Techniques and Applications*, pp.51-63 (Marcel Dekker, Inc., New York, 1987)].

Please amend the paragraph on page 36, beginning on line 4 to read as follows:

To obtain a cDNA encoding full-length PSTPIP tagged with the FLAG epitope (DYYDDDDK) (SEQ ID NO:8) at the C-terminus, PCR was performed using primers 48.BAMHI.F (CGCGGATCCACCA TGATGGCCCAGCTGCAGTTC) (SEQ ID NO:9) and 48.SALFLAG.R (GTACGCGTCGACTCACTrGTCATCGTCGTCC TTGTAGTCGAGCTD (SEQ ID NO:10). The resulting PCR fragment was digested with BamHI and Sal I and subcloned into the BamHI and Sal I sites of pRK.tkneo, an expression plasmid containing the cytomegalovirus promoter, thus creating plasmid pRK.PIP.FLAG.C. The PTP HSCF deletion mutants were derived from a construct containing the influenza hemagglutinin epitope at its N-terminus and were made as follows: PCR was performed on PRK.HSCF using primers prkr (TGCCTTTCTCTCCACAGG) (SEQ ID NO: 11) and 38.spe.mid.R (CTCCTTGAGGTTCTACTAGTGGGGG CTGGTGTCCTG) (SEQ ID NO:12). The resulting PCR fragment encoding the phosphatase domain (amino acids 1-312) was digested with Cla I and Spe I and subcloned into pRK.tk.neo digested with Cla I and Xba I resulting in plasmid pRK-hscf.ptp domain. Similarly, PCR using primers prkr and 39.spe endR (GCGGCCGCACTAGTATCCAGTCTG TGCTCCATCTGTTAC) (SEQ ID NO: 13) was performed and the resulting fragment encoding amino acids 1-439 of hscf was digested with Cla. I and Spe I and subcloned into the Cla I and Xba I sites of pRKtkneo. GST fusion proteins were prepared essentially according to the manufacturer (Pharmacia Biotech) in DH5-alpha bacterial cells. A Sal I to Not I fragment containing the full-length cDNA for PSTPIP (amino acids 2-415) was subcloned into pGEX4T-2 (~~Pharmacia~~ Pharmacia™) cleaved at the Sal I and Not I sites.

Please amend the paragraph on page 36, beginning on line 35 to read as follows:

The binding was carried out according to the method of Wong and Johnson (Wong et al., *J. Biol. Chem.* 271(35):20981-20984 (1996)). Briefly, 1 μg of plasmid with

either the PSTPIP protein or PTP HSCF under the control of the Sp6 promoter was *in vitro* transcribed/translated using the ~~Promega~~ Promega™ TnT Rabbit ~~Reticulocyte~~ Reticulocyte™ system. Samples were diluted in 50 mM HEPES, pH 7.2, 1% triton X 100, 10% glycerol, 100mM NaCl, 5mM EDTA and 2 μg/ml each of leupeptin, pepstatin, aprotinin, and PMSF. Samples were pre-cleared with resin for 1 hour and 1 μg GST-fusion protein was added along with 30 μl of GSH-Sepharose that was previously blocked in 3% BSA for 1 hour. This was reacted for 1 hour at 4°C and then the resin washed 6 times in HEPES/Triton binding buffer before SDS gel electrophoresis. The peptides were synthesized on an automated Milligen 9050 Peptide Synthesizer using standard solid phase chemistry with FMOC protected amino acids on a p-alkoxybenzyl alcohol resin. Dried peptides were re-suspended in the HEPES/Triton Binding buffer at a concentration of 10 mg/ml. Peptide inhibition was performed by adding the peptide first to the *in vitro* translation product and then the GST-fusion followed by the GSH-Sepharose. The binding/washing steps were as previously described. The peptides synthesized and the PTPs they were derived from were:
PXXP-HSCF: $_{432}$GFNLRIGRPKGPRDPPAEWT$_{451}$ (PTP HSCF) (SEQ ID NO:20),
PXXP-PEP: $_{782}$GFGNRFSKPKGPRNPPSAW$_{800}$ (PTP PEP) (SEQ ID NO:21),
PXXP-PEST: $_{761}$GFGNRCGKPKGPRDPPSEWT$_{780}$ (PTP PEST) SEQ ID NO:22),
PXXP-CONTROL: $_{334}$GGVLRSISVPAPPTLPMADT$_{353}$ (PTP HSCF) (SEQ ID NO:23).

Please amend the paragraph on page 37, beginning on line 32 to read as follows:

COS-7 cells were transfected by electroporation. Briefly, 1.5 x 10^6 COS-7 cells were mixed with 24 μg total DNA in PBS and electroporated at 960μF, 0.22 volts (~~Bio-Rad Gene Pulsar~~ Bio-Rad™ Gene Pulsar™). Following electroporation, cells were seeded in 10cm dishes and incubated for 3 days. 10-cm dishes of transfected COS cells were washed twice with ice-cold PBS, and lysed in 1ml of M-RIPA (50mM Tris 7.4,

1% NP40, 0.25% DOC, 150mM NaCl, 1mM sodium ortho-vanadate, 1mM NaF plus Complete™ Protease Inhibitors (Boehringer Mannheim)). Lysates were incubated for 15 minutes with 100µl UltraLink Immobilized Protein ~~A/G~~ A/G™ (Pierce) at 4°C, followed by centrifugation for 5 minutes. Supernatants were collected and stored at -70°C or directly immunoprecipitated. 5 µg of M2 or 12CA5 was added to 500 µl of lysate and incubated overnight at 4°C. Ultralink Protein ~~A/G~~ A/G™ was added and incubation continued for 2 hours at 4°C. The immune complexes were washed 3 times with M-RIPA. The proteins were subjected to SDS-PAGE and transferred to nitrocellulose in 1X Transfer ~~Buffer~~ Buffer™ (Novex). Immunoblots were blocked overnight at 4°C in 3% milk/PBS. To detect Flag-tagged PIP, blots were incubated with 10µg/ml Bio-M2 (Biotinylated anti-FLAG monoclonal Ab, KODAK) followed by incubation in 10µg/ml streptavidin-HRP (UBI). To detect HA-tagged PTPhscf, blots were incubated in anti-(HA)-peroxidase (Boehringer Mannheim) as per manufacturer's instructions. To detect phosphotyrosine, blots were incubated in HRP-conjugated 4G10 (anti-phosphotyrosine monoclonal, UBI) as per manufacture's instructions.

Please amend the paragraph on page 38, beginning on line 10 to read as follows:

Rabbit polyclonal antibodies were produced against a GST-PSTPIP fusion protein. The complete PSTPIP-GST fusion protein was purified on GSH-sepharose and injected intramuscularly at 2 sites with 200 µg fusion protein and subcutaneously at multiple sites with a total of 300 µg PSTPIP-GST fusion protein in Complete Freunds Adjuvant. Rabbits were boosted every 3 weeks with 100 µg fusion protein in Incomplete Freunds. 15 ml of rabbit sera was reacted with 0.5mg PSTPIP-GST-GSH-Sepharose for 3 hours at 4^0C with gentle rotation. The resin was collected by centrifugation and washed with 10 column volumes of PBS. Immunoglobulin was eluted from the affinity matrix with 100mM acetic acid, 500mM NaCl, neutralized with NaOH, and then dialyzed overnight with PBS. NIH 3T3 cells were seeded at 100,000 cells per

chamber slide and allowed to adhere overnight. The cells were transfected using ~~Lipofectamine~~ Lipofectamine™ (2ug pRK.PIP.FLAG.C/12 ul Lipofectamine in 0.8ml OPTI-MEM) for 5 hours. The ~~DNA/ Lipofectamine~~ DNA/Lipofectamine™ solution was removed and fresh serum containing medium added. 48 hours following the start of transfection, the cells were fixed in 4% formaldehyde in PHEM 6.1 (60mM PIPES, 25mM HEPES, 10mM EGTA and 2mM $MgCl_2$) for 20 minutes, then permeabilized in 0.2% Triton X-100, 300mM sucrose in PHEM 6.9 for 10 minutes. The cells were washed twice in PHEM 6.9 and then incubated with 10% FBS/PHEM 6.9 for 1 hour to block non-specific binding of the antibody. Cells were incubated for 1 hour in 2% BSA/PHEM 6.9 containing 10μg/ml M2 (KODAK, anti-FLAG monoclonal antibody) or 10μg/ml 12CA5 (Boehringer Mannheim anti-HA monoclonal antibody) as an irrelevant antibody control. After washing cells twice with 2% BSA/PHEM6.9, cells were incubated with for 30 minutes with a 1:2000 dilution of Cy3-conjugated ~~AfinniPure~~ AfinniPure™ sheep anti-mouse IgG and a 1:200 dilution of Fluorescein Phalloidin (Molecular Probes) in 2% BSA/PHEM 6.9. Cells were washed in 2% BSA/PHEM6.9 and mounted in ~~Vectashield Mounting Medium~~ Vectashield Mounting Medium™ with DAPI. NIH3T3 cells were seeded at 200,000 cells per chamber slide and allowed to adhere overnight. Cells were stained with 0.4μg/ml rabbit anti-PIP or 0.4μg/ml rabbit IgG and detected with Cy3-corjugated goat anti-rabbit. Additionally, cells were co-stained with a 1:200 dilution of Fluorescein-Phalloidin.

Please amend the paragraph on page 45, beginning on line 4 to read as follows:

Confocal microscopy was performed as previously described (Spencer *et al*, (1997), *supra*). Briefly, CHO cells in chamber slides were transfected using Lipofectamine and the indicated plasmids. 48 hours later, cells were fixed in formaldehyde and stained with an anti-FLAG epitope specific antibody (Kodak) and Fluorescein-Phalloidin (Molecular Probes). Anti-Flag stained cells were washed and stained with Cy3-conjugated sheep anti-mouse IgG. Stained cells were observed using

a ~~Molecular Dynamics Confocal Microscope~~ Molecular Dynamics Confocal Microscope™ (2001) and analyzed with ~~ImageSpace~~ ImageSpace™ software (Molecular Dynamics).

Please amend the paragraph on page 46, beginning on line 19 to read as follows:

The mutagenesis of PST PIP was accomplished using the Dut/Ung$^-$ procedure (~~BioRad~~ BioRad™ Laboratories, Richmond CA). The mutagenesis primers were designed to change 3 contiguous amino acids to alanine. Mutations were spaced approximately 12 amino acids apart, with new restriction sites engineered in for identification of mutant clones. Primer annealing was carried out at 70°C for 10 minutes, 37°C for 10 minutes, room temperature for 5 minutes, then on ice prior to T7 DNA polymerase addition, The primers used for PST PIP alanine scan mutagenesis were (all 5' to 3'):

D_{38}VE: GTCTGAGGAGCTCCGCCGCAGCCTTGCAC, (SEQ ID NO: 43)

E_{50}ER: CCTTCCCGTACGCCGCCGCCGCCTGAGCTCTCTG (SEQ ID NO: 44)

R_{62}K: GGCCACCAGCCGCGGCTGCAATCTGCACGAGC (SEQ ID NO: 45)

R_{73}TS: CAGGGAGTCAAAGGCGGCCGCCAGGGAGTTCATC (SEQ ID NO: 46)

N_{84}VG: CTGGATGTGCGCGCTGGCCGCAGCCTCTGTTTGC (SEQ ID NO: 47)

R_{99}EE: CCTCCAAGCTTCGCAGCGCCGCAGCCAGGGCCAGGGC (SEQ ID NO: 48)

E_{110}RQ: CCGCTGCTCTTTCGCTGCCGCTCGGAATTCCTCC (SEQ ID NO: 49)

I_{122}MD: CTTCTGGACACGGGCCGCGGCGGCCTCATACTTCT (SEQ ID NO: 50)

L_{132}YK: GGTCTTCTTGGCGGCCGCAAGCTTGCTCTTCT (SEQ ID NO: 51)

D_{145}QK: GCATCCCTGCACGCCGCGGCATATAAGCTTTCTTGGACTCCA
(SEQ ID NO: 52)

E_{159}RV: GTGGCCATTGGCACTCGCAGCCGCGAAAGCTTGCTCAGCATC
(SEQ ID NO: 53)

Q_{169}VE: GGCTTTGTTCTGGCTCTTTGCTGCTGCCTTCTGGTGACCATTGGC

(SEQ ID NO: 54)

R_{194}QN: CCTCGCTCTCTCCAGTTGTTCAATAGCTGCCGCGCGTACACTCT

SEQ ID NO: 55)

W_{204}: CTCCTGCTCCGCCTCGGTCCGAGCTCTCC (SEQ ID NO: 56)

F_{221}: GGATGGTGAGCCGGTCTGCCTCCTGCAGCTGGAGGCC (SEQ ID NO: 57)

L_{224}: CGGAGGATGGTGGCCCGGTCGAATTCCTGCAACTGG (SEQ ID NO: 59)

W_{232}: ATGGAGAGCTGGTTACAGTGCACCGCCAATGCATTGCGGAGG

(SEQ ID NO: 59)

Cysteines within the region of PTP HSCF binding domain of PST PIP were also mutated to alanine using the following primers (all 5' to 3'):

CYS_{36}: TCCACATCCTTGGACATCTTCCTG (SEQ ID NO: 60)

Cys_{148}: CATCATCTGCATCCCTGGCCTTCTGGTCATATCCCTTCTTG

(SEQ ID NO: 61)

Cys_{180}: GGCTGACTCCTTGGACTGCTTGGC (SEQ ID NO: 62)

CYS_{213}: GAAGGCCTCGGAGGTAGTCCGGTGCTC (SEQ ID NO: 63)

CYS_{235}: ATGGAGAGCTGGTTGGAGTGCACCCACA (SEQ ID NO: 64)

$CY5_{242}$: CATCATCCTTGACGGACTGCATGGAGAGCT (SEQ ID NO: 65)

Cys_{259}: GATGTCACCTTCCACATCGGAGCCCTCAAGGGTCAG

(SEQ ID NO: 66)

Please amend the paragraph on page 59, beginning on line 13 to read as follows:

Expressed poly-his tagged PSTPIP can then be purified, for example, by Ni^{2+}-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature 362: 175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL, Hepes, pH 7.9; 12.5 mM $MgC1_2$; 0.1 mM EDTA; 10% Glycerol; 0.1% NP-40; O4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the

supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% Glycerol, pH 7.8) and filtered through a 0.45 ;μm filter. A Ni^{2+}-NTA agarose column (commercially available from ~~Qiagen~~ Qiagen™) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A_{280} with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% Glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or western blot with Ni^{2+}-NTA-conjugated to alkaline phosphatase (~~Qiagen~~ Qiagen™). Fractions containing the eluted His_{10}-tagged PSTPIP are pooled and dialyzed against loading buffer.

Amendments to the Sequence Listing:

The following peptide sequences disclosed in Figure 13 as originally filed have been added to the Sequence Listing in this application:

LGFNLRIGRPKGPRDPPAEWT (SEQ ID NO: 74)

IGFGNRCGKPKGPRDPPSEWT (SEQ ID NO: 75)

GFGNRFSKPKGPRNPPSAW (SEQ ID NO: 76)

An amended Sequence Listing is enclosed which includes in electronic copy the amino acid sequences shown in Figure 13.